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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,616	10/30/2001	Mads Gruenberg	20780 US (C38435/0124164)	6580
7590 02/16/2006 BRYAN CAVE LLP 33RD FLOOR 1290 AVENUE OF THE AMERICAS NEW YORK, NY 10104			EXAMINER WHALEY, PABLO S	
			ART UNIT 1631	PAPER NUMBER

DATE MAILED: 02/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/016,616	Applicant(s) GRUENBERG ET AL.	
	Examiner Pablo Whaley	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 09 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
 4a) Of the above claim(s) 2,5 and 9-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4 and 6-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>Mar. 12, 2002</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

APPLICANTS' ELECTION

Applicants' election of Group I drawn to Claims 1-8, and election of Species I-B (an optimization routine) and Specie I-D (CO₂ transfer rate) with traverse, filed 01/09/2006, is acknowledged. However, because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The specie election drawn to a parameter (Specie I-D) is hereby withdrawn for the expedience of prosecution. Claims 2, 5, and 9-16 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 01/09/2006.

CLAIMS UNDER EXAMINATION

Claims herein under examination are Claims 1, 3, 4, and 6-8.

PRIORITY

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the European Patent Office (EPO) on 10/31/2000. It is noted, however, that applicant has not filed a certified copy of the application as required by 35 U.S.C. 119(b).

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OBJECTIONS

Claim 6 is objected to because of the following informalities: Claim 6 is grammatically incorrect, and should recite "wherein a ratio...is treated as a separate control variable but is adjusted simultaneously." Appropriate correction is required.

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 4, and 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites a "new feed concentration" in line 6. The term "new" feed concentration implies that an initial feed concentration was supplied or determined previously, however no such step limitation is recited in the claims. Clarification is requested. Claims 3, 4, and 6-8 are rejected as they depend from claim 1.

Claim 1 recites a "method of optimizing performance of a bioprocess" in the preamble. It is unclear in what way the steps of the instant claim achieve the purpose of the preamble, as it is unclear where a bioprocess' performance is optimized. Clarification is requested.

Claim 1 recites the limitation "periodically and alternately" in line 3. It is unclear what "alternates." Clarification is requested.

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Claim 4 recites the limitation "a co-ordination controller." It is unclear exactly what elements are being "co-ordinated" by this controller, and in what way this controller generates a flow chart using a negative-pulse response technique. Clarification is requested.

Claim 4 recites the limitation "the input variable." There is insufficient antecedent basis for this limitation. Furthermore, it is unclear as to what this input variable represents and what this input variable is input to. Clarification is requested.

Claim 6 recites the limitation "a ratio...are treated as separate control variables." It is unclear exactly what elements are being treated as separate control variables. Clarification is requested.

Claim 6 recites the limitation "the feed concentrations." There is insufficient antecedent basis for this limitation.

CLAIM REJECTIONS - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application

filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 4, 7, and 8 are rejected under 35 U.S.C. 102 (b) as being anticipated by Fleury et al. (Advances in Bioprocess Engineering, 1994, p.313-320).

Fleury et al. teach modeling and control strategies for the transformation of D-sorbitol to L-Sorbose (Abstract). More specifically, Fleury et al. teach the following aspects of the instantly claimed invention:

- Control system with multiple feed pumps supplying nutrients (s_1 , s_2 , H_2O) to a microorganism [Fig. 2], as in instant claim 1(a).
- Implementation of a delay before starting control actions to allow a minimal convergence of the state observer to values near the “real” state vector [p.318, col. 2, lines 28-34 and Fig. 4], which correlates to “periodically and alternately stopping a supply of each nutrient...until a metabolic activity of the microorganism decreases by a preset percentage” as in instant claim 1(a). Note the state vector is a representation of product and nutrient concentrations represented as percentages (Fig. 4).
- Calculation of new feed concentration values [Table 3], as in instant claim 1(b).
- Use of a non-linear model to design a control strategy for nutrient delivery [p.317, col.1, lines 21-32], which correlates to an optimization routine as in instant claim 1(c).
- Use of sorbitol and yeast extract (s_1 , s_2) [p.314], which correlates to a complex nutrient mixture with different nutrients as in instant claim 3.
- Use of the microorganism *Gluconobacter oxydans* (i.e. *suboxydans*) [p.313, col. 1, paragraph 1], as in instant claim 7.

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- Microbial oxidation of D-sorbitol to L-sorbose [p.313, col. 1, paragraph 1], as in instant claim 8.
- Optimization routine generating a flow chart using negative-pulse response [p.319, col. 2, Fig. 5], as in instant claim 4(a).
- Time-variant flow charts of controlled and non-controlled systems with demonstrating negative-pulse response (Fig. 4 and Fig. 5), as in instant claim 4(a), (b).
- Control actions involving feed pumps using time values [Fig. 1], as in instant claim 4(c).

Claims 1, 3, and 4 are rejected under 35 U.S.C. 102 (a) as being anticipated by Miskiewicz et al. (Biotechnology Letters, 22: 1685-1691, 2000).

Miskiewicz et al. teach a fuzzy logic controller to control nutrient dosage in a fed-batch yeast process (Abstract). More specifically, Miskiewicz et al. teach the following aspects of the instantly claimed invention:

- Fragmented nutrient dosage [Fig. 7 and Fig. 8], which correlates to periodically and alternately stopping a nutrient supply as in instant claim 1(a).
- Portion-wise complex nutrient dosage to a microorganism culture when a dissolved O₂ concentration reactor changes by a set value (45%) [p.1686, col. 2, lines 1-6], which correlates to instant claim 1(a).
- Calculation of consecutive nutrient dosage based on multiple inputs using a fuzzy logic controller [p.1686, col. 2, lines 24-26], which correlates to adjusting the amount of nutrient supplied as in instant claim 1(b).

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- Use of a fuzzy logic controller to supervise nutrient feed inflow and provide optimum yield [p. 1685, col. 2, paragraph 2; and p.1686, col. 1, paragraph 1], which correlates to an optimization routine as in instant claim 1(c).
- Complex nutrient mixture containing more than one nutrient [p. 1686, col. 1, lines 9-14], as in instant claim 3.
- Fragmented nutrient dosage process controlled by a fuzzy logic controller demonstrating negative-pulse response [Fig. 8], which correlates to instant claim 4(a).
- Determination of nutrient size (i.e. pulse) and points in time at which the dosage of consecutive nutrient portions should be start [p.1691, col. 1, lines 4-9], which correlates to instant claim 4 (b), (c).
- Nutrient amounts and rates as inputs into fuzzy logic controller [p. 1686, col. 2, lines 11-24] and calculation of time of cycle [Fig. 2], which correlates to instant claim 4(c).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

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made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 4, and 6-8 are rejected under 35 U.S.C. 103(a) as being obvious by Kurokawa et al. (Biotechnology And Bioengineering, Vol. 44, No. 1, 1994), in view of Johnson et al. (US Pat. No. 6,792,336; Filed: May 13, 1999) and Fleury et al. (Advances in Bioprocess Engineering, 1994, p.313-320).

Kurokawa et al. teach the use of an adaptive control algorithm to simultaneously control glucose and glutamine concentrations (Abstract). More specifically, Kurokawa et al. teach the following aspects of the instantly claimed invention:

- Positive, negative, and zero slope feed rates [Fig. 3], which correlates to alternately and periodically starting and stopping nutrient supply as in instant claim 1(a).
- On-line measuring and controlling system with multiple feed peristaltic pumps controlled by a computer [Fig. 1], which correlates to instant claim 1(a). Note: any computer controlled pump can be programmed to periodically and alternately stop nutrient supply.
- Simultaneous supply of at least complex nutrient mixtures [p.96, col. 2, lines 1-3], as in instant claims 1(a) and 3.
- Adjusting feed rates to decrease inhibitory metabolite activity by a certain concentration [p.99, col. 1, paragraph 2], which correlates to instant claim 1(a).
- Adaptive control algorithm for correcting the feed rate from real-time data at every sampling time [p.98, col. 2, lines 29-32], which correlates to instant claims 1(b) and (c).
- Generation of time-variant flow charts and response times based on three control algorithms [Fig. 2 and 3], as in instant claim 4(a) and (b).

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- Using response times (i.e. sampling times) as input variables [p.97, Equation (7)], as in instant claim 4(c).
- Separate and simultaneous adjust of nutrient feed rates and concentrations [Fig. 3(b) and (c)] and [Table II], which correlates to instant claim 6.

Kurokawa et al. do not specifically teach the use of a "microorganism", but do suggest the use of such control models with fermentation processes involving microorganisms [p.95, col. 2, paragraph 3].

Johnson et al. teach the use of learning-based control systems using multiple or difficult to characterize parameters [Abstract]. Johnson et al. further teach: (i) fuzzy logic computer-controlled pumps for nutrient feeds [31]; (ii) a culture of minerals-processing microorganisms [9]; and (iii) the optimization of nutrient flow rates for the newly selected set points [29].

Fleury et al. teach a multi-feed system and modeling and control strategies for the transformation of D-sorbitol to L-Sorbose using the microorganism *Gluconobacter oxydans* (i.e. *suboxydans*) [p.313, col. 1, paragraph 1], as discussed previously.

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the invention of Kurokawa et al. with the use of the fuzzy logic control system of Johnson et al. and the microorganism *Gluconobacter oxydans* as taught by Fleury et al., where the motivation would have been to increase productivity by developing an optimized process which adapts to the metabolic response of an industrially useful microorganism while varying multiple control parameters simultaneously [Johnson et al., (18),(31)], resulting in the practice of the instant claimed invention with a reasonable expectation of success.

CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**MARJORIE A. MORAN
PRIMARY EXAMINER**

Marjorie A. Moran
2/13/06